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# New CEO Focuses on Advancing Antibody Drugs to Fight Alzheimer's Disease and Other Neurodegenerative Conditions

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**CEOCFO:** ***Mr. Warma, what is the concept behind ProMIS Neurosciences?***
**Mr. Warma:** ProMIS is focused on treating neurodegenerative diseases, specifically the treatment of multiple dementias. We have a novel proprietary platform that is directed to the treatment of many multiple diseases that cause destruction and damage to the brain and the central nervous system.

**CEOCFO:** ***You recently took on the CEO role, moving from board member. What do you see at ProMIS that led you to take this on this new position?***
**Mr. Warma:** There were three things I noticed when I joined the board 2.5 years ago and these have become more prominent now that I have joined ProMIS as CEO just over a month ago. The primary thing that excites me about the company is our science, which is truly differentiated and novel. The second is our people. We have assembled a superb team of highly experienced experts in drug development and the treatment of neurodegenerative diseases.

The third thing that excites me about the opportunity is the potential to make a difference in the lives of patients suffering with multiple neurodegenerative diseases. Because of the broad application of our platform, we have been able to develop a robust pipeline of drug candidates with our lead drug candidate now in clinical development. Therefore, the science, the team, and the potential across multiple neurodegenerative diseases are the three things that excite me about the company.

**CEOCFO:** ***What is the science at ProMIS?***
**Mr. Warma:** It is an elegant science that was developed by Dr. Neil Cashman, one of the leading researchers in the field and our Chief Scientific Officer. Dr. Cashman has pioneered the science for several years. Simply put, we use AI to target specific forms of toxic, harmful proteins. Proteins are continuously manufactured by the cells to perform multiple useful day-to-day functions throughout an individual's life. However, these complex protein structures often become malformed or misfolded and begin to build up or aggregate in the body, which leads to harmful effects and disease progression.

Typically, misfolded proteins are cleared from the body by the immune system. However, if the immune system becomes weak or as a person ages, it is not able to clear these misfolded toxic proteins quickly enough. Through our technology, we have developed an antibody drug that identifies these toxic misfolded proteins, homes in on specific binding sites of those proteins and binds to the toxic proteins to clear them from the body -- in our specific case to clear them from the brain.

The focus is to help the body clear these toxic misfolded proteins from the body because if they are not cleared, and they are allowed to continue to form, they will clump together and form aggregates. Then, they become highly toxic and lead to disease progression in multiple disease states. It is a unique approach that we apply to these toxic misfolded proteins.

**CEOCFO:** ***How do you find them?***
**Mr. Warma:** This is the brilliance of Dr. Cashman's and the scientific team's work. They take a physics and algorithmic approach to identify the misfolded proteins. We know which proteins are associated with specific diseases, so we look at certain proteins involved with Alzheimer's, Parkinson's, or ALS. We can identify the proteins and predict when they are going to misfold and can distinguish unique binding sites that are present only on the misfolded proteins.

Our specificity in binding is unique to ProMIS because we do not want it to bind anywhere else. We only want our drug to bind specifically and only to the misfolded, toxic proteins. It is our novel AI algorithmic approach that is proprietary to ProMIS and which allows us to bind only the toxic misfolded protein associated with that specific disease.

**CEOCFO:** ***Is the medical community onboard? Do they understand the concept? What are some competing approaches and how do they compare?***
**Mr. Warma:** The medical community is very much on board with this. The harmful effect of these misfolded proteins is well known and documented throughout the literature and the publications. Many diseases are associated with these misfolded proteins, not only neurodegenerative diseases, but also cancer, for example. Scientifically, the medical community understands the relevance and the harmful effects of misfolded proteins. The complication is how to specifically target the misfolded protein. A good example is Alzheimer's disease, where the goal is to target the amyloid beta (Aβ) protein. There are different forms of A-beta that exist in the body; some of them are

beneficial and some are harmful. For some, it is not known if they are relevant to disease or not. As you can imagine, it is easier to make a drug that binds all forms of A-beta than to distinguish between the multiple forms, which is very challenging. Therefore, if a drug binds all forms, there may be a modest beneficial effect because you are targeting the toxic form but there may also be a serious downside if the drug binds beneficial forms of A-Beta such as monomers or the plaque form, which has been associated with serious brain swelling and bleeding.

This is where ProMIS' technology is differentiated – it's our ability to bind and target the toxic oligomers in Alzheimer's disease. It is challenging to specifically bind only the toxic form of the protein given that multiple forms of these proteins exist. ProMIS is unique in that we can identify not only the protein but the specific form of that protein. For example, PMN310 does not bind the monomeric form of A-beta as monomers are beneficial to the body. It also does not bind to the plaque form of A-beta. It is not certain whether clearing plaque actually improves clinical outcomes but we have seen that clearing plaque is associated with significant side effects including swelling and bleeding in the brain. Therefore, our goal is to avoid the monomers and the plaque and just target the toxic oligomers. Our proprietary algorithmic approach gives us the precision and selectivity to only eliminate the toxic form of the protein. In the case of Alzheimer's disease, we target and remove the A-beta misfolded toxic monomer. We expect that with this level of specificity, we should see improved efficacy and a better safety profile with PMN310.

**CEOCFO:** ***It seems to me in the general discussions of AI that it is well-received in the medical community and that this is a good use of AI!***
**Mr. Warma:** Yes, very much so. In our case, the use of AI refers to our computational, algorithmic approach that streamlines, simplifies, and accelerates drug development tremendously. It allows us to identify the unique binding sites on the misfolded protein and to design an antibody drug candidate within six months. It clearly speeds up our processes and allows us to generate multiple candidates to build our pipeline.

**CEOCFO:** ***Where are you right now in development and commercialization?***
**Mr. Warma:** It is certainly the most exciting time of our development because we are in the clinic running human studies with our lead candidate, PMN310, which is currently in a Phase 1 clinical study. In drug development, the most important data are generated from human clinical studies and we started our first human clinical trial in November 2023. We are moving very well through the Phase 1a portion of that clinical trial, which is being conducted in the US. This study is being evaluated in healthy volunteers to establish safety.

The other important data point of the trial is evaluating the level of antibody drug (PMN310) that crosses into the central nervous system (CNS). We will be measuring the drug level of PMN-310 in the cerebral spinal fluid (CSF) to determine how well it can cross the blood-brain barrier and get into the CNS. This will enable us to predict whether the

drug will bind to its target in patients. Therefore, there are two key data points in this first clinical study. One is safety and one is levels of drug in the CSF to indicate target binding for future studies. It is exciting for us to be in patients and, ideally, once the Phase 1a portion of the study is completed, we expect to roll into the Phase 1b portion of the study in Alzheimer's disease patients.

If we are successful in demonstrating safety and efficacy in patients, this will not only provide proof-of-concept for our lead drug in Alzheimer's disease, but will also validate the broader platform, where we have several candidates in development and are close to entering the clinic. For example, ALS and Parkinson's disease are two diseases we are interested in developing in the future. As I said, it is a very exciting time for the company.

**CEOCFO:** ***How do you decide what comes next; what are your criterion?***
**Mr. Warma:** For us, there are several things we think about when considering next steps. We look at unmet medical needs across all these diseases: ALS, Alzheimer's, Parkinson's, and Schizophrenia; each representing significant unmet medical needs. Beyond that, we look at the cost and the time to demonstrate proof-of-concept with our drug candidate. We also consider the regulatory landscape and the complexity of the clinical development program required. In addition, we evaluate the competitive landscape and the level of competition in the various diseases, which indicates whether it is an opportune moment to move into that space.

We also look at how interested and active the large pharmaceutical companies are in these disease areas as our goal is to partner with them to undertake those longer-term studies. We want to be able to excite and interest global pharma companies to collaborate with us in the future. So, as you can see, there are several elements that go into identifying and prioritizing which indications we select to move forward with.

**CEOCFO:** ***There are several large global companies with approved products on the market; how do you compete and does the name matter or does the concept itself stand out to the public?***
**Mr. Warma:** I do not see this as a competition, it is more complimentary. I think the advances in Alzheimer's disease drug development in the past couple of years--with a few of these drugs being approved-- is superb. There was a long drought in Alzheimer's disease drug development where there were no new drug approvals, so these approvals over the last couple of years have been promising. These are always stepwise improvements, there never has been a one-off cure for these diseases. The large global companies realize the potential of the drugs they are bringing to market but they are also looking for other breakthrough drugs to complement the work they are doing.

What we might see in the future is combination therapies for Alzheimer's disease. For example, the drugs that have recently come to market have

a positive effect but some of them are associated with severe safety issues that make treating these patients and prescribing these drugs very challenging. While there are advances in the treatment of Alzheimer's disease, there is still a long way to go in finding additional drugs that show improvement above and beyond what is currently available on the market. This is why these companies look to other players, such as ProMIS, to say, "What are you developing." ProMIS' unique approach, which avoids binding to plaque and specifically targets the toxic oligomers, is something that is really exciting in the industry in general.

While the company name is important when considering collaborations, it is more important to consider which one is a better fit and has the commitment and motivation to work with our novel drug. There are a number of companies already in the Alzheimer's space and others that are eager to move into this disease area. These are companies that we see very much as partners. We are not looking to compete with these large companies. Rather, we are seeking to collaborate with them to form synergistic partnerships to advance our molecules through Phase 3 and to market. They have the muscle to get to market and we have the novel science that can get them there.

**CEOCFO:** ***What has been the reaction from the investment community and what should they be looking at going forward; what are the benchmarks?***
**Mr. Warma:** The reaction from the scientific community has been very positive over the past couple of years and we have also seen momentum build from the investor community since the beginning of the year. 2024 has seen a strong start in the biotech and biopharma markets, following a couple of challenging years. This past month or two we have seen more interest across the board in biotech/Pharma deals, especially in the neuroscience therapeutic area, which bodes well for ProMIS.

For us specifically, I think a lot of people are excited now that we are in the clinic. Once we start getting human safety and proof-of-concept data, this interest should grow exponentially. This could be when we see a significant value inflection. Once data become available, which is expected in the near-term, we should start to unlock this potential. Over the coming months – not years – we should see some exciting data that we expect will validate our approach and create value. Beyond that, we plan to expand into other disease indications as I mentioned earlier. I am pleased with the conversations I am having with investors and potential partners and believe they view our platform as particularly promising and truly differentiated. This is key because you have to have a differentiated product or nobody, whether it is an investor, pharma company, patient, or physician, is going to be interested.

For me personally, when I get involved with any company, I focus on whether this is a differentiated product and novel science. ProMIS certainly is and we are starting to see the investment community take notice of our ability to uniquely target these toxic oligomers in Alzheimer's disease, which to date, no other company has been able to do selectively. Consequently, why we believe we are seeing an uptick in interest in our very promising platform.

**CEOCFO:** ***Final thoughts?***
**Mr. Warma:** The next three to six months will be interesting for us as we complete the first part of the Phase 1 study and advance our lead compound through development for the treatment of Alzheimer's disease. We expect initial clinical data from the Phase 1a study to be available in the middle of the year, so in the next several months we should have our first clinical data from that study and, ideally, we would like to move quickly into the second half of the Phase 1 study -- the multiple ascending dose portion of the study in Alzheimer's disease patients. Data from this second portion of the Phase 1 study should be available by the end of next year.

For your readers, they should see this as a very promising opportunity as we expect to unveil our first data from the Phase 1a study in the next few months, which should position us to demonstrate proof-of-concept over the next twelve to eighteen months in Alzheimer's disease patients.

If this study demonstrates proof-of-concept for our lead product in Alzheimer's, it unlocks the value of the entire pipeline. Given today's valuation, we strongly believe there is a significant disconnect between our current valuation and the potential of this company. If we can unlock some of this potential in the coming months, I think investors, pharma companies, and, most importantly, patients will start to realize the value ProMIS is creating as a promising treatment for multiple dementias and neurodegenerative diseases.